

## Invited Speaker Abstract

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### **Bisphosphonate use in osteoporosis, benefits and risks**

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Bisphosphonates are the most commonly used first-line therapy for osteoporosis. Structurally similar to naturally occurring pyrophosphate, they have a high affinity for calcium hydroxyapatite crystals. Bisphosphonates are targeted drugs with a high specificity for osteoclasts. They potently inhibit bone resorption by interfering with osteoclast function and inducing osteoclast apoptosis. Bone formation is also reduced. Once sequestered in bone, bisphosphonates are slowly released with a variable half-life. Clinically, they reduce vertebral, non-vertebral and hip fractures and improve quality of life. Administration of intravenous zoledronic acid following a hip fracture also reduced subsequent mortality.

Bisphosphonates are well tolerated and the rate of adverse events is very low. Upper gastrointestinal events, including gastric irritation, oesophageal erosions, and gastric ulcers are associated with oral administration, but are less likely with weekly dosing regimens. Such side effects can be related to pre-existing gastroesophageal reflux or failure to remain upright after dosing. Serious adverse events are more common with higher doses or when elimination is impaired and may differ in frequency depending on the route of bisphosphonate administration. Renal impairment, osteonecrosis of the jaw (ONJ), atrial fibrillation, musculoskeletal pain and unusual femoral diaphyseal fractures (related to low bone remodelling) have recently been uncommonly associated with bisphosphonate treatment. ONJ occurs rarely, but is a potentially serious event in patients treated for osteoporosis. It has an estimated frequency of 1:10,000-100,000, however, is seen more frequently in patients with multiple myeloma or bony metastases treated with higher total doses of intravenous bisphosphonates. Its aetiology is uncertain, but there is a strong association with periodontal disease and dental extraction, highlighting the need for collaboration with dental practitioners. The cause of atrial fibrillation associated with bisphosphonate use is unknown, but it may be more common with intravenous zoledronic acid.

The benefit-risk profile strongly favours the use of bisphosphonates in osteoporosis.